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Case Report

Perforation of the sigmoid colon secondary to localised amyloidosis

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Amyloidosis is a heterogeneous group of disorders characterised by systemic or localised extracellular deposition of an abnormal protein material in the interstitium of organs and tissues, often resulting in functional impairment.

Although the gastrointestinal tract is susceptible to the deposition of amyloid materials with systemic disease, localised amyloidosis of the gut is very rare.[1] Complications associated with amyloidosis of the gastrointestinal tract are uncommon and colonic perforation is exceptionally rare. We report a case of perforation of the sigmoid colon secondary to localised amyloidosis and review other reports in the literature.

CASE REPORT An 88 year-old male patient presented with an acute onset of severe generalised abdominal pain. Over the previous five years he had undergone investigation for episodes of abdominal pain and rectal bleeding. Previous endoscopic examinations had revealed both sessile polyps and areas of ulceration in the sigmoid colon. Biopsies on each occasion had demonstrated colonic amyloidosis. He had no other relevant past medical history.

On admission, he was distressed but apyrexial. Abdominal examination revealed generalised tenderness with marked guarding and rebound, and absent bowel sounds. Rectal examination revealed no abnormalities. Initial haematological investigations and abdominal X-rays were normal.

At laparotomy he was noted to have generalised faecal peritonitis with a perforated sigmoid colon. The remainder of the colon and small bowel was grossly normal. A Hartman's procedure was performed and the peritoneal cavity was thoroughly lavaged. Postoperatively, he was treated with intravenous antibiotics and made a satisfactory recovery.

The gross specimen consisted of a 26 cm length of sigmoid colon which showed focal mucosal ulceration, perforation with a surrounding serosal reaction and marked thickening of the bowel wall

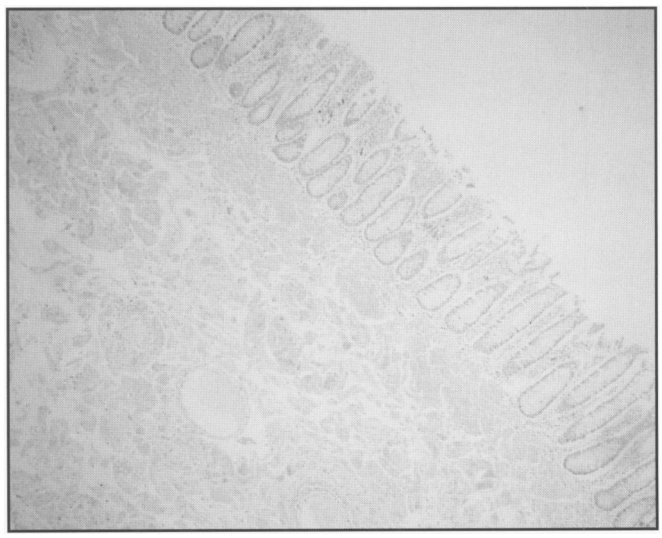

Fig 1. Congo red stain demonstrating submucosal amyloid (Magnification x 144).

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over a 15 cm segment. In addition, there was a 0.5 cm adenomatous polyp. Histology revealed mucosal ulceration and expansion of the submucosa by amorphous eosinophilic material (fig 1) which also extended between smooth muscle bundles in the muscularis propria. This material resembled amyloid histologically. There was a localised peritonitis adjacent to which deposits of amyloid were also present (fig 2). Congo red staining was positive both before and after treatment with potassium permanganate (KMnO4) and the typical apple green birefringence on examination under polarized light was observed. Immunohistochemistry showed lambda (λ) light chain positivity but

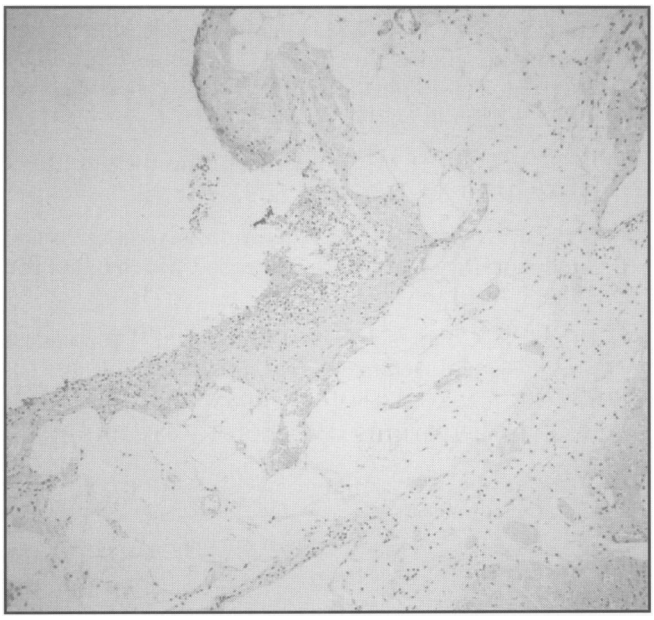

Fig 2. Haematoxylin and eosin preparation demonstrating serosal deposition of amyloid and evidence of peritonitis (Magnification x 60).

negativity with Kappa (κ) light chain, AA protein, AP protein and Transthyretin. Electron microscopy showed rigid non-branching fibrils 10-15 mm in diameter in keeping with amyloid.

Subsequent investigations to exclude other concomitant conditions revealed an ESR of 30 mm/hr, normal plasma protein electrophoresis and urine testing was negative for Bence Jones proteins.

DISCUSSION

Many classifications of amyloidosis have been proposed. In general, however, amyloidosis can be divided into two categories – systemic and localised. The systemic category, which commonly involves the gastrointestinal tract, includes primary (idiopathic) amyloidosis, secondary (reactive) amyloidosis (occurs in association with chronic inflammatory conditions, such as rheumatoid arthritis, ankylosing spondylitis, connective tissue disorders, tuberculosis, osteomyelitis, neoplasia or inflammatory bowel disease), amyloidosis associated with multiple myeloma or other plasma cell dyscrasias and familial types of amyloidosis. The protein deposited in primary (AL) amyloidosis is a normal immunoglobulin light chain (intact or N-terminal fragments of Igκ or Igλ) that is overproduced by an aberrant B-cell clone. In reactive (AA) amyloidosis the protein deposited is a normal serum protein, amyloid A component (AA), an acute-phase reactant that is produced in the liver in response to inflammation. Overproduction of transthyretin is indicative of senile amyloidosis or familial types of amyloidosis. Dialysis-associated amyloid is associated with the accumulation of β2-microglobulin.

Localised amyloidosis is site-limited and does not progress to systemic involvement. It commonly affects the skin, respiratory tract or genitourinary tract. The gastrointestinal tract is rarely involved, with fewer than 20 cases reported in the literature. Congo Red staining and its resultant green birefringence when viewed with high intensity polarised light, is pathognomonic for amyloidosis. The potassium permanganate (KMnO4) method or immunohistochemistry may be used to investigate amyloid protein types. Failure of pre-treatment with KMnO4 to abolish Congo Red positivity is more in keeping with AL amyloid, but it is not specific. The amyloid deposits in this case showed positivity for lambda (λ) light chains using immunohistochemical techniques. Although this is commonly associated with systemic amyloidosis, it is also often seen in localised amyloidosis. In view of the absence of detectable abnormal proteins in the serum and urine, and since other chronic inflammatory conditions, such as collagen diseases and multiple myeloma were excluded, this case was diagnosed as localised amyloidosis of the gastrointestinal tract.

Histopathologically, deposits of amyloid are either found in and around the walls of small submucosal blood vessels or within the mucosal layer and/or muscular layers of the gut wall. In most cases, the submucosal blood vessels are the

earliest and most frequent site of amyloid deposition. This can lead to blood vessel narrowing or occlusion, with resulting ischaemia, infarction or perforation.

Gastrointestinal amyloidosis, whether systemic or localised, can present in a variety of ways. The commonest symptoms of amyloidosis affecting the large bowel are abdominal pain, rectal bleeding, weight loss and watery diarrhoea, however, involvement of the intestinal musculature may cause pseudo-obstruction. Intestinal infarction, ischaemic colitis and mass lesions mimicking malignancy have all been reported. Intestinal perforation is an exceptionally rare complication with only six previous reports in the literature.[2-7] This patient had been noted on previous endoscopic examinations to have had both sessile polyps and areas of ulceration in the sigmoid colon and subsequently presented with perforation secondary to severe ulceration.

Localised amyloidosis is essentially a benign condition; however, systemic amyloidosis is almost invariably fatal and treatment is mainly supportive. Death usually follows a cardiac event or renal failure. Median survival in primary systemic amyloidosis is between 12 and 15 months and most patients succumb within 3 years of diagnosis.[8] In amyloidosis associated with multiple myeloma the prognosis is even worse, with a median survival of only 4 months.[8] Outlook is better for secondary amyloidosis where survival up to 5 years is common [9] and there are occasional case reports documenting long-term survival. No specific therapy is available, however, for systemic forms of amyloidosis; treatment of the underlying disease is of prime concern.

Surgical intervention for amyloidosis affecting the gastrointestinal tract should be reserved for emergency procedures only, such as in patients with massive bleeding, perforation or obstruction, as there may be an associated haemorrhagic diathesis, or anastomotic dehiscence resulting from poor local healing. In the present case, the diagnosis had been made five years previously, but active surgical intervention was undertaken only when the patient presented with an acute abdomen.

REFERENCES

1. Matsui H, Kato T, Inoue G, Onji M. Amyloidosis localized in the sigmoid colon. *J Gastroenterol* 1996; **31(4)**: 607-11.
2. Heitzman E J, Heitzman G C,Elliot C F. Primary esophageal amyloidosis: report of a case with bleeding, perferation and survival following resection. *Arch Intern Med* 1962; **109(5)**: 595-600.
3. Akbarian M, Fenton J. Perforation of small bowel in amyloidosis. *Arch Intern Med* 1964; **114(12)**: 815-21.
4. Griffel B, Man B, Kraus L. Selective massive amyloidosis of small intestine. *Arch Surg* 1975; **110(2)**: 215-7.
5. Ioachim N J, McKenna P J, Delaney W E, Toth I, Chung F J. Cryoglobulinemia and amyloidosis associated with intestinal lymphoma. *Arch Intern Med* 1978; **138(7)**: 1158-60.
6. Gonzalez Sanchez J A, Martin Molinero R, Dominguez Sayans J, Jimencz Sanchez F. Colonic perforation by amyloidosis: Report of a case. *Dis Colon Rectum* 1989; **32(5)**: 437-40.
7. Gilat T, Spiro H M. Amyloidosis and the gut. *Am J Digest Dis* 1968; **13(7)**: 619-33.
8. Kyle R A, Greipp P R. Amyloidosis (AL). Clinical and laboratory features in 229 cases. Mayo Clin Proc 1983; 58(10): 665-83.
9. Hind C R K, Pepys M B. Amyloidosis: [3] Diagnosis, prognosis and treatment. *Hospital Update* 1984; **10**: 737-48.